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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,496	10/15/2004	Roy Christiaan Montijn	101137-55	4628

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EXAMINER

WOOD, AMANDA P

ART UNIT	PAPER NUMBER
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1657

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/511,496	Applicant(s) MONTIJN ET AL.	
	Examiner Amanda P. Wood	Art Unit 1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 July 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's response and amendments filed 13 July 2007 have been received and entered.

Claims 1-13 have been examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In particular, claim 1 recites the phrase "determining an environmental condition of which the effect on one or more microorganisms is unknown comprising measuring a natural biochemical composition...where said composition specifically changes...the induction route that leads to the change in the biochemical composition is unknown, comparing said biochemical composition to a predetermined calibration line of a plurality of biochemical compositions of said one or more microorganisms." Claims 2 and 3 recite nearly identical claim language to that of claim 1, particularly the limitations that the effect of the environmental condition on the microorganism is unknown and that the induction route that leads to the change in the biochemical composition is unknown. In addition, claim 13 recites the phrase, "determining an environmental condition without identification of the effect of such environmental condition on one or more microorganisms comprising measuring a natural biochemical composition" in lines 1-4. It is

unclear how one of skill in the art would be expected to know what natural biochemical composition to measure in said microorganism if the effect of the environmental condition on said microorganism is not identified. In addition, it is unclear how one of ordinary skill in the art would be expected to determine an environmental condition in which a microorganism has been placed if the effect of the environmental condition on said microorganism is unknown (i.e., what to measure for is unknown) and if it is also unknown what leads to the change (i.e., what is the induction route or what condition causes the change). Furthermore, Applicant has given no guidance in the instant specification as to how one of ordinary skill in the art would determine what natural biochemical composition to measure, and whether the biochemical composition is something found in a microorganism, or in the environment. With respect to the instant specification, Applicant merely states (on page 3, lines 14-17) that "in principle, a large number of environmental conditions can be deduced therefrom, in principle without it being necessary that the induction routes that lead to the change are known." Applicant has provided no clear examples in the instant specification teaching one of skill in the art how to make and use the invention, as claimed. In addition, Applicant has given no guidance as to how one of skill in the art would determine an environmental condition, or determine a change in an environmental condition without knowledge of how the condition affects the microorganisms which are being exposed to it, and furthermore, without such knowledge, it would require undue experimentation to determine what biochemical compositions, and therefore, biomolecules, would need to be measured, to make the necessary measurements for practice of the instantly claimed invention (i.e., how would one of skill in the art know where to begin with measuring biomolecules?).

All other claims depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, first paragraph for the reasons set forth above.

Response to Arguments

Applicant's arguments filed 13 July 2007 have been fully considered but they are not persuasive. In particular, Applicant argues that one of skill in the art would know what environmental condition to measure because it will cause effects, causing a difference in the measured biochemical composition compared with the calibration set of biochemical compositions. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that an environmental condition will cause a difference in the measured biochemical composition compared with the calibration set of biochemical compositions) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant recites "calibration line" in the claims and specification, but no "calibration sets" of biochemical compositions. Furthermore, Applicant argues that it would be within the skill and scope of one skilled in the art to determine which biochemical compositions to measure. The Examiner respectfully disagrees with Applicant's argument, because the claimed subject matter of measuring "a plurality" of biomolecules and determining an environmental condition based upon that is of such a broad scope that it would require undue experimentation for one of skill in the art to determine even where to begin measuring biomolecules, since it appears from the language of the claims that even the environmental condition is unknown.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the phrase measuring a natural biochemical composition by detecting qualitatively or quantitatively a plurality of different biomolecules..." in lines 3-4. Claims 2 and 3 recite nearly identical claim language to that of claim 1, particularly the limitations involving measuring a biochemical composition by detecting biomolecules. It is unclear whether the biomolecules being detected are components of the natural biochemical composition, or whether they are something made by the microorganism in response to the presence of the biochemical composition and/or due to exposure to the environmental condition, or are something else entirely. Furthermore, Claims 1, 2, and 3 recite the phrase "the induction route that leads to the change in the biochemical composition is unknown, comparing said biochemical composition to a predetermined calibration line of a plurality of biochemical compositions of said one or more microorganisms." It is unclear what exactly Applicant means by the term "induction route" and how one of skill in the art would be expected to know what biochemical composition to measure in a particular microorganism, what change in said composition to measure, and under what conditions said measurement should be made, in order to practice the claimed invention. Furthermore, it is unclear from the wording of the claims for what particular microorganisms a plurality of biochemical compositions are predetermined in a calibration line (i.e., are they the same or different microorganisms as in the preamble and/or in line 6 of claim 1?). In addition, claim 13 recites the phrase, "determining an environmental condition without identification of the effect of such environmental condition on one or more microorganisms comprising measuring a natural biochemical composition" in lines 1-4. It is

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unclear how one of skill in the art would be expected to know what natural biochemical composition to measure in said microorganism if the effect of the environmental condition on said microorganism is not identified.

All other claims depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, second paragraph for the reasons set forth above.

Based upon the indefinite nature of the instant claims, a further search was unable to be performed on the claims. Therefore, the following references appear to be the closest prior art.

Response to Arguments

Applicant's arguments filed 13 July 2007 have been fully considered but they are not persuasive. Applicant argues that there is no one biochemical composition to be measured in the claims, that the claims require a plurality of biochemical compositions to be measured, but the Examiner respectfully disagrees. The claims specifically require "measuring a natural biochemical composition." A plurality of biochemical compositions is only involved in the calibration line. Furthermore, Applicant argues that claim 13 is not indefinite because multiple biomolecules are measured and then compared to see if they have changed upon exposure to the environmental condition, but the Examiner still asks how does one of skill in the art know which biomolecules or biochemical composition to select as a starting point for measuring if it is not known what effect an environmental condition has on a microorganism?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-13 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Larossa et al (US 6,607,885).

A method for determining an environmental condition of which the effect on one or more microorganisms is unknown by measuring a biochemical composition of one or more microorganisms exposed to said environmental condition is claimed.

Larossa et al beneficially teach a method wherein the effect of environmental changes are determined by measuring gene expression levels (i.e., the transcriptome) in bacteria. Larossa et al specifically teach that *E. coli* experiments to define stress-related responses in the past have used mRNA measurements to determine an individual gene's expression profile (see, for example col. 1, lines 30-60 and col. 2, lines 20-65).

In addition, Larossa et al beneficially teach a method wherein a bacterial species is subjected to a gene expression altering condition (i.e., an environmental condition) and a microarray of the bacterial RNA is generated so as to identify the gene expression level and changes in the bacteria. Furthermore, Larossa et al beneficially teach that it is possible to monitor the effect of environmental changes on gene expression by comparing expression levels of genes from bacteria that have not been exposed to stress to those of bacteria that have been exposed to stress. Larossa et al further teach a method to be used as a modeling system to test for perturbations in process conditions

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to provide a method as disclosed by Larossa et al, with respect to the art-recognized method of using microorganisms to monitor an environmental condition or changes in a condition, as discussed above. In addition, the cited reference particularly points out that microarrays can be used to determine the amount of RNA or protein a microorganism, such as bacteria, expresses upon exposure to a stressor, such as a change in environmental condition, and therefore, it would have been both obvious and beneficial for the skilled artisan to use the methods taught by Larossa et al so as to determine an environmental condition by measuring a plurality of biochemical compositions of one or more microorganisms. The result-effective adjustment of particular conventional working conditions (e.g., using a particular microorganism and/or using a particular method to determine the biochemical composition) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole, was *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the cited references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicants' arguments concerning the above USC 103 rejection have been carefully considered but are not deemed to be persuasive of error in the rejection. Applicant does not provide any arguments with respect to Larossa et al, even in the reply to the first Office Action in which Larossa et al appeared (26 April 2006), Applicant merely argued that Larossa et al did not

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cure the deficiencies of Duncan et al, and did not specifically point out any problems with the Larossa et al reference.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda P. Wood whose telephone number is (571) 272-8141. The examiner can normally be reached on M-F 8:30AM -5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

APW



CHRISTOPHER R. TATE
PRIMARY EXAMINER